REMARKS

The Office Action has objected to Claim 68 alleging that it is duplicative of Claim 61. Furthermore, the Office Action has rejected Claims 69-71 under 35 U.S.C. §112, second paragraph, as allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Further, the Office Action has rejected Claims 56-61 and 66-67 under 35 U.S.C. §102(b) as defining subject matter which is allegedly anticipated by the teaching in WO 97/41856, of which Lansbury et al. are inventors. In addition, the Office Action has rejected Claims 56-64 and 66-71 under 35 U.S.C. §103(a) as defining subject matter which is allegedly rendered obvious by the teachings of Lansbury et al. in view of the teachings of U.S. Patent No. 5,004,697 to Pardridge ("Pardridge"). Finally, Claims 56-71 are rejected under 35 U.S.C. §103(a) as defining subject matter which is allegedly rendered obvious by the teachings of Lansbury et al. in view of Pardridge and further in view of an article by Prokopchuk et al. in Organometallics, 1999, 18(15), 2861-2866 ("Prokopchuk et al.").

Applicants have amended the claims, which when considered with the comments hereinbelow, are deemed to place the present case in condition for allowance. Favorable action is respectfully requested.

Applicants have amended the claims by deleting therefrom the metal complexes of 2, 2'-bipyridine. However, Applicants have not abandoned the subject matter therein and reserve the right to file a continuation application directed thereto. In addition, the dependency of Claim 68 was changed to Claim 67. Further, Claim 62 was amended to recite the complex comprises or is conjugated to targeting a moiety, consistent with original Claim 62. Claims 66 and 71 were amended to correct grammatical errors.

Applicants have also added Claims 72-74. Support can be found in original Claim 16. Claims 69-71 are amended, respectively, to be dependent thereon.

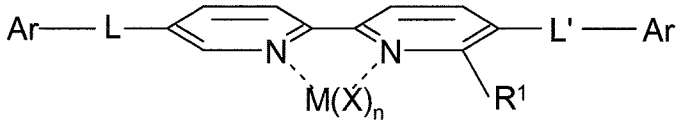
No new matter has been added to the application.

The Office Action has objected to Claims 61 and 68, alleging that they are substantially duplicative. Applicants have amended Claim 68 to be dependent on Claim 67. Thus, as amended, the claims are not duplicative. Therefore, this objection is overcome; withdrawal thereof is respectfully requested.

Pursuant to the rejection of Claims 69-71 under 35 U.S.C. §112, the Office Action alleges that the term "targeting moiety" lacks antecedent basis. Claims 69-71 are dependent upon Claims 72-74 which specifically recites therein "that the complex comprises or is conjugated to a targeting moiety. Thus, this is a sufficient antecedent basis for "targeting moiety" in claims 69-71. Therefore, this rejection is overcome; withdrawal thereof is respectfully requested.

Pursuant to the rejection of Claims 56-61 and 66-68, the Office Action cites Lansbury et al.

According to the Office Action, Lansbury et al. teach the use, *inter alia*, of 2,2' bipyridine compounds of the formula



wherein M is, *inter alia*, Cd, Co, Cu, Ni, Zn, Fe or ^{99}Tc, ^{111}In, ^{90}Y or ^{186}Re.

However, the claimed subject matter does not include any metal complexes of bipyridines. Case law has held that anticipation requires the reference to disclose each and every element of the claims, either explicitly or implicitly. Verdegaal Bros. v. Union Oil Co. of

California, 814 F2d 628, 631, 2 USPQ2d 1051, 1053 (Fed Cir 1987). The absence of an element of the invention in a prior art reference negates anticipation by the reference. Kalman v. Kimberly Clark Co. 713 F2d 760, 771-772, 218 USPQ 781, 789 (Fed Cir 1993).

Further, Lansbury et al. do not teach or disclose any metal complex with a porphyrin or 1, 10-phenanthroline, as claimed. The claimed subject matter does not include a bipyridine complexed to a metal, and therefore, the claimed subject matter does not contain an element of the subject matter described in Lansbury et al. Thus, the claimed subject matter is not anticipated by the teachings in Lansbury et al.; withdrawal of this rejection is respectfully requested.

Pursuant to the rejection of Claims 56-64 and 68-71 under 35 U.S.C. §103(a), the Office Action cites Lansbury et al. and Pardridge.

The Office Action reiterates its comments with respect to Lansbury et al. It alleges that Pardridge teaches modifying antibodies for delivery through the BBB for neuropharmaceuticals, and that the antibody is for the amyloid peptide of Alzheimer's disease.

According to the Office Action, Lansbury et al. teach treating Alzheimer's disease with a metal bipyridine complex, but it does not teach its coupling with a targeting moiety. The Office Action alleges that Pardridge provides the missing element. It concludes that it would have been obvious to make and deliver a bipyridine complex to the Alzheimer's plaques that it is used to treat.

Applicants reiterate the comments hereinabove with respect to Lansbury et al. Although Lansbury et al. may teach a bipyridine coupled with a metal, it does not teach, disclose or suggest the use of a metal complex of a porphyrin or a 1, 10- phenanthroline, as claimed.

Pardridge does not overcome the shortcomings of Lansbury et al. As described in the Office Action, Pardridge teaches modifying antibodies for delivery through the blood brain barrier for neuropharmaceuticals. It, however, does not teach, disclose or suggest the use of a metal complex of a porphyrin or a 1, 10- phenanthroline, as claimed. Even assuming, *pro arguendo*, that the combination of Lansbury et al. and Pardridge suggest complexing an antibody with a metal complex of bipyridine, as alleged by the Office Action, the combination does not teach, disclose or suggest complexing or conjugating a targeting moiety to a metal complex of phenanthroline or porphyrin, such as an antibody with a neutral complex of 1, 10-phenanthroline or porphyrin, as claimed. A review of both Lansbury et al. and Pardridge quickly reveals that neither teach nor disclose a metal complex with or conjugated to a porphyrin or a 1, 10-phenanthroline. Thus, since neither Pardridge or Lansbury et al. teach, disclose or suggest a metal complex with 1, 10-phenanthroline or porphyrin, the combination of those references cannot teach, disclose or suggest the use of a metal complex of 1, 10-phenanthroline or porphyrin for treating Alzheimer's disease or for inhibiting the binding of one or more metal ions to a ß-amyloid protein, as claimed. Thus, this rejection under 35 U.S.C. §103 is obviated; withdrawal thereof is respectfully requested.

Pursuant to the rejection of Claims 56-71 under 35 U.S.C. §103(a), the Office Action cites Lansbury et al. in view of the teachings of Pardridge and further in view of the teachings of Prokopchuk et al.

The Office Action reiterates its comments with respect to Lansbury et al. and Pardridge.

According to the Office Action, Lansbury et al. teach a variety of metal complexes, except Pt, that are taught to be useful for treating Alzheimer's disease. However, the

Office Action indicates that Lansbury et al. do not teach, disclose or suggest the use of Pt as the metal.

It cites Prokopchuk et al. for its teaching of platinum 2,2'-bipyridine complexes as well as 1, 10-phenanthroline complexes. It does not teach any porphyrin metal complex.

According to the Office Action, it would have been obvious to have used any metal, including Pt, in the complex with bipyridine. The Office Action notes that Ni, Pd and Pt are in the same period. According to the Office Action, "Given that Ni, Pd and Pt are in the same period and that Lansbury [et al.] explicitly contemplated a variety of transition metals, including Ni and other elements, sharing similar oxidation state to Pt (and the other claimed transition metals), one would reasonably expect any transition metal would function in the complex of Lansbury [et al.] to treat Alzheimer's."

Applicants reiterate the comments hereinabove with respect to Lansbury et al. and Pardridge. As indicated hereinabove, the combination does not teach, disclose or suggest the use of a metal complex of 1,10-phenanthroline or porphyrin with Mn, Co, Ni, Cu, Ru, Pd, Ag, Cd, Pt, Au, Ph or Hg, and/or the use of this metal complex additionally comprising and/or conjugated to a targeting moiety, as claimed.

Prokopchuk et al. do not overcome the shortcomings of the combination of Lansbury et al. and Pardridge. Prokopchuk discloses that a platinum complex Pt Me_2(9N3)], where 9N3 is 1,4,7-triazacyclononane, undergoes protonation by triflic acid and reversibly, even by methanol to form the cationic complex [Pt HMe_2 9N3)]$^+$. It teaches that oxidation of either compound by H_2O_2 gives the hydroxy complex [Pt(OH)Me_2(9N3)]$^+$, which can be reversibly protonated to the aqua complex [Pt$(OH)_2Me_2$(9N3)]$^{2+}$.

The teachings of Prokopchuk et al. are limited to the aforementioned Pt complexes. Further, it provides no utility for the complexes therein. Since Lansbury et al. do not teach that Pt complexed with bipyridine can be used to treat Alzheimer's disease, it is mere speculation by the USPTO that any platinum complexes described in Prokopchuk et al. would be useful for treating Alzheimer's.

Inasmuch as neither Lansbury et al. nor Pardridge not Prokopchuk et al. disclose any utility of the Pt complexes, it cannot be assumed that the Platinum 1,10-phenanthroline compounds can be used to treat Alzheimer's disease or that it can be used to inhibit the binding of one or more metal ions to a ß-amyloid protein, as claimed. Case law has held that although the close structural similarity of compounds gives rise to the presumption that the skilled artisan would expect these compounds to possess similar properties, there is no presumption where no usefulness is disclosed for prior art compounds. In re Stemmski, 444 F2d 581, 587, 170 USPQ 343, 347 (CCPA 1971). Thus, based on case law, the combination does not suggest that Pt complexed 1,10-phenanthroline or bipyridine can be used to treat Alzheimer's disease or inhibit the binding of one or more ions to a ß-amyloid protein, contrary to the allegation of the Office Action.

Inasmuch as the combination does not teach, disclose or suggest that a metal complex of 1,10-phenanthroline or porphyrin, as claimed, can be used to either inhibit binding of one or more metals to a ß-amyloid peptide or to treat Alzheimer's disease, the combination does not teach, disclose or suggest the present utility, as claimed.

Moreover, although Pt is in the same period as Pd and Ni, Applicants respectfully submit that it is not true that it can be substituted for these other metals. For example, Pt is considered to have high toxicological properties that must be managed in its use for the treatment

of cancer, e.g., in the form of cisplatin. As platinum compounds cause apoptosis of cells through changes in DNA structure, which inhibits DNA replication, transcription and cell division, compounds containing this metal are not an obvious choice for the skilled person seeking to treat Alzheimer's disease.

However, assuming, *pro arguendo*, that the teachings of Lansbury et al. could be combined with Prokopchuk et al. in the manner suggested by the Office Action, the combination would suggest, at most, that metal complexes of bipyridine would be useful for treating Alzheimer's disease. However, the claimed subject matter does not include bipyridine complexes. Thus, the combination does not teach, disclose or suggest the present invention.

Therefore, for the reasons given, this rejection under 35 U.S.C. §103 is obviated; withdrawal thereof is respectfully requested.

Thus, in view of the Amendments to the Claims and the comments hereinabove, it is respectfully submitted that the present case is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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